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10/063,557	05/02/2002	Dan L. Eaton	GNE.3230R1C39	9770

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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,557	EATON ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/10/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendment received 9/9/02 has been entered in full.

2. Claims 1-6 are pending and under examination.

Specification

3. The disclosure is objected to because of the following informalities:

a. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. For example, see page 31, line 15 and page 35, line 7. Applicant is required to check the entire disclosure and delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01

b. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

Oath/Declaration

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the citizenship of each inventor. The actual citizenship status for inventors Mary E. Gerritsen and Audrey Goddard is unclear because "CA" is

not a recognized country and does not adequately identify the actual citizenship status.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific and substantial asserted utility or a well-established utility.

The claims are directed to antibodies that bind a polypeptide corresponding to SEQ ID NO:50, referred to in the specification as PRO1069. The utility and enablement of the antibody depends upon whether or not the polypeptide it binds has utility and enablement. The specification discloses that PRO1069 is a transmembrane polypeptide (see Figure 2) and the nucleic acid (DNA59211-1450) encoding the PRO1069 polypeptide is more highly expressed in normal kidney as compared to kidney tumor (see page 141 of the disclosure), however, there is no direct correlation between a specific disease state and the expression of the PRO1069 polypeptide. The specification does not assert that PRO1069 has or shares any particular biological activity or function with any known polypeptide. The specification generally asserts that all of the disclosed PRO polypeptides will be useful for a number of purposes; however, none of these asserted uses meet the "specific" and "substantial" utility requirement of 35 U.S.C. § 101. The asserted utilities will each be addressed in turn.

1) the PRO polypeptide can be used to isolate other polypeptides to which it binds: this asserted utility is not specific or substantial. Since the same can be done

with any polypeptide, the asserted utility is not specific to the claimed PRO1069 polypeptides. Furthermore, since the specification does not disclose how PRO1069 or its binding partners can be used, significant further research would be required of the skilled artisan to determine how to use the claimed polypeptide or its binding partner. Since the asserted utility is not presented in a ready to use, real-world application, the asserted utility is not substantial.

2) the PRO polypeptide can be used as a molecular weight marker: this asserted utility is not specific. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1069 polypeptide.

3) the PRO polypeptide can be used in tissue typing: this asserted utility is not specific or substantial. With the exception of a few housekeeping genes, all polypeptides have a tissue specific pattern of expression, and thus virtually any polypeptide can be used in tissue typing. Thus, the asserted utility is not specific to PRO1069. Furthermore, the tissue-specific pattern of expression for PRO1069 is not disclosed. The skilled artisan would have to determine the tissue specific pattern of expression empirically. Thus, the asserted utility is also not substantial.

4) the PRO polypeptide can be used in therapy: this asserted utility is not specific or substantial. Since a defect in any polypeptide is likely to cause a disease of some sort, every polypeptide is a target for drug development. Thus, the asserted utility is not specific to the claimed PRO1069 polypeptide. Furthermore, the specification does not disclose a nexus between any specific disease states and a change in amount or form

of PRO1069. Significant further research would have to be conducted to identify such a nexus. Therefore, the asserted utility is not substantial.

5) the PRO polypeptide can be used to identify agonists or antagonists: since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1069 polypeptide. Furthermore, since no activity has been assigned to PRO1069, the assays cannot be conducted until the specific biological activities of PRO1069 are determined empirically. Thus, the asserted utility is also not substantial, as the real-world use has not been established.

Therefore, the specification does not support a specific and substantial asserted utility or a well-established utility regarding the claimed antibodies because the PRO1069 polypeptide to which the antibodies bind does not have a specific and substantial asserted utility or a well-established utility. The proposed antibodies of the claimed invention are simply starting points for further research and investigation into potential practical uses of the PRO1069 polypeptide. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 are indefinite for reciting "an antibody that binds" in claim 1 and "the antibody of claim 1 which specifically binds" in claim 6 because the exact meaning is unclear. It is not clear what the difference between the two claims is and what each claim is meant to encompass, given that antibody binding is determined by the variable regions structure and is a "specific" interaction.

10. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They

include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to an antibody that binds or specifically binds the PRO1069 polypeptide (i.e., SEQ ID NO:50), wherein the antibody is monoclonal, humanized, an antibody fragment and labeled.

The specification teaches that the nucleic acid of DNA59211-1450, which encodes the PRO1069 polypeptide was more highly expressed in normal kidney as compared to kidney tumor in gene amplification assays (see Example 18, pages 140-144). The specification asserts that anti-PRO antibodies would be useful in diagnostic assays (see page 112).

The specification does not teach that the PRO1069 polypeptide is expressed, either over-expressed or under-expressed in any disease state.

The specification does not reasonably provide enablement for antibodies that bind the PRO1069 polypeptide from the written disclosure alone. Those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. In fact, evidence abounds in which protein levels do not correlate with steady-state mRNA levels or alterations in mRNA levels. For example, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of

p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Further, Powell et al (Pharmacogenetics, 1998, Vol. 8, pp. 411-421, abstract) teach that mRNA levels for cytochrome P450 E1 did not correlate with the level of corresponding protein, and conclude that the regulation of said protein is highly complex. Vallejo et al (Biochimie, 2000, vol. 82, pp. 1129-1133, abstract) teach that no correlation was found between NRF-2 mRNA and protein levels suggesting post-transcriptional regulation of NRF-2 protein levels. Lewin B. (Genes VI, 1997, CH. 29, pp. 847-848) states "But having acknowledged that control of gene expression can occur at multiple stages, and that production of RNA cannot inevitably be equated with production of protein, it is clear that overwhelming majority of regulatory events occur at the initiation of transcription" (see page 847, right column). These references serve to demonstrate that the analysis of levels of polynucleotide transcripts cannot be relied upon to anticipate levels of protein expression. Further, Jang et al (Clinical and Experimental Metastasis, 1997, vol. 15, pp. 469-483, abstract) teach that further studies are necessary to determine if changes in protein levels track with changes in mRNA levels for metastasis associated genes in murine tumor cells, thus providing further evidence that one of skill in the art cannot anticipate that the level of a specific mRNA expressed by a cell will be paralleled at the protein level due to complex homeostatic factors controlling translation and post-translational modification.

Thus, the predictability of protein translation and its possible utility as a diagnostic or therapeutic target are not necessarily contingent on the levels of mRNA

expression due to the multitude of homeostatic factors affecting transcription and translation. Therefore, absent evidence of the PRO1069 polypeptide expression, including the correlation to a diseased state, one of skill in the art would not be able to predictably use antibodies that bind the PRO1069 polypeptide as a diagnostic or therapeutic tool. The specification does not predict or show whether the PRO1069 polypeptide would be over-expressed or under-expressed in a specific, diseased tissue compared to the healthy tissue control. In the absence of a direct correlation between the up regulation of transcription and translation of the PRO1069 polypeptide associated with a disease state, one of ordinary skill in the art would be unable to use antibodies specific for the PRO1069 polypeptide.

No direction or guidance is provided to assist one skilled in the art to make and use the claimed antibodies that bind the PRO1069 polypeptide in any diagnostic or therapeutic setting. Thus, the proposed use of the claimed antibodies that bind the PRO1069 polypeptide are simply starting points for further research and investigation into potential practical uses of the polypeptide. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field" and "a patent is not a hunting license" "[i]t is not a reward for the search, but compensation for its successful conclusion."

In view of the lack of predictability of the art to which the invention pertains as evidenced by Fu et al., Powell et al., Vallejo et al., Lewin B. and Jang et al., and lack of guidance in the specification related to using antibodies that bind or specifically bind the PRO1069 polypeptide, undue experimentation would be required to practice the claimed antibodies with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed antibodies and absent working examples providing evidence which is reasonably predictive that the claimed antibodies are effective as a diagnostic or therapeutic tool correlated to a specific disease state.

Priority

11. The examiner acknowledges the priority statement filed 9/9/02, however, because the claimed subject matter does not have a specific and substantial asserted utility or a well-established utility, the priority date of the claims are given the filing date of the instant application, 5/2/02.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-2 and 4-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Lal et al (WO 00/00610, published 1/6/00).

Claims 1-2 and 4-6 are drawn to an antibody that binds or specifically binds the PRO1069 polypeptide (i.e., SEQ ID NO:50), wherein the antibody is monoclonal, an antibody fragment and is labeled.

Lal et al teach a polypeptide (SEQ ID NO:35), which is identical to the instantly claimed polypeptide of SEQ ID NO:50 (see attached sequence alignment on the back of this Office Action) and antibodies that bind the polypeptide are monoclonal, antibody fragments and labeled (see pages 44-45 and 52-53).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lal et al (WO 00/00610, published 1/6/00) as applied to claims 1-2 and 4-6 above, and further in view of Queen et al (U.S. Patent 5,530,101, issued 6/96).

The claims are drawn to an antibody that binds or specifically binds the PRO1069 polypeptide (i.e., SEQ ID NO:50), wherein the antibody is monoclonal, humanized, an antibody fragment and labeled.

Lal et al have been described supra. Lal et al does not teach a humanized antibody. This deficiency is made up for in the teachings of Queen et al.

Queen et al teach humanized antibodies (see entire document).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized antibody to the polypeptide of Lal et al in view of Queen et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a humanized antibody to the polypeptide of Lal et al in view of Queen et al because Lal et al teach the polypeptide of SEQ ID NO:50 (i.e., SEQ ID NO:35 of Lal et al) is found in humans and it would be obvious in view of Queen et al who teaches humanized antibodies for detection in humans (see column 20, lines 23-33).

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at (571) 272-0827 from 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

Official papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The official fax number for Group 1600 where this application or proceeding is assigned is (703) 872-9306.

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER